Statement By

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Coalition for a Stronger FDA

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INTRODUCTION

Mr. Chairman and members of the Committee, I am William K. Hubbard. Before my retirement after 33 years of Federal service, I served for many years with the U.S. Food and Drug Administration, and for my last 14 years was an FDA Associate Commissioner responsible for, among other things, FDA's regulations and policy development. Although I remain retired since my departure from FDA in 2005, I serve as an advisor to The Coalition for a Stronger FDA, a consortium of patient, public interest, and industry organizations whose mission is to urge that FDA's appropriations be increased. The Coalition and its constituent members are greatly concerned that FDA's resource limitations have hampered the agency's ability to ensure the safety of our food and drug supply. Today's hearing is a timely example of one of those concerns—the massive increase in pharmaceuticals being imported into the United States at a time in which FDA's capacity to oversee those foreign producers is in serious doubt. Accordingly, I wish to thank the Committee for inviting me to testify on that subject today.

BACKGROUND

As you know, Congress created the current regulatory structure for assuring the safety of human drugs in 1938, through its enactment of the Food, Drug and Cosmetic Act. That statute recognized that drugs could be a key component of our health care system, but that drugs were also powerful chemicals with the capability to produce great harm if not carefully regulated. Thus Congress determined it necessary to create a relatively

pervasive regulatory system which requires that drugs be carefully tested before being approved for marketing, and produced under exacting quality control standards. Subsequent FDA regulations have provided specific requirements for drug manufacturers to meet in carrying out Congress's direction. So, today, drugs are cautiously tested, first in animals, then in humans, and approved by FDA only if their medical benefits outweigh any risks they pose. Once approved for marketing, a drug must be manufactured under specific controls mandated by FDA—known as Good Manufacturing Practices. These include requirements that active ingredients of the drug be of a prescribed purity, strength and quality; that the drug be made in well controlled, sanitary conditions; that its labeling and packaging be equally well controlled; and that laboratory tests of the drug be performed routinely using well established scientific methods and properly calibrated equipment to confirm that the drug is always produced in the form approved by the FDA.

A RECORD OF REMARKABLE SUCCESS

The result of this regime established by Congress and implemented by the FDA has been unsurpassed, and perhaps unequaled, in my opinion, by any American industry. FDA now approves new drugs as fast or faster than any other country in the world (thanks to the user fee program enacted by this Committee). The high standards for drug safety and efficacy that you and the FDA have demanded have led to a cascade of new discoveries across the decades that have placed the U.S. pharmaceutical industry far above foreign competitors in quantity and quality of new therapeutics. Indeed, countries around the world look to the FDA as the "gold standard" for determining if a new drug should be

approved and for establishing safe manufacturing controls for marketed drugs. Today, physicians, pharmacists, and their patients have a very, very high confidence that the drugs they prescribe, dispense, and use are well understood, well made, and will perform as expected.

THE GLOBAL SITUATION

The portrait of pharmaceuticals elsewhere around the world is not so positive. Drugs developed and produced in other countries do not always have the same record of therapeutic success as American pharmaceuticals. But perhaps more importantly, unlike the relatively closed U.S. drug market, in most countries these products are subject to normal arbitrage, which means that drugs move about much as do electronics, apparel, auto parts and thousands of other goods. This has meant that drugs are often purchased from suppliers who have little or no oversight by regulatory bodies; that key elements of safe drug production are ignored—such as quality testing, expiration dating, and labeling controls; and that producers of substandard and counterfeit drugs have a relatively easy access to the marketplace.

Specific examples of dangers in the international drug market abound. Let me list just a few:

- The recent substitution of ethylene glycol (antifreeze) for pharmaceutical grade glycerin in an elixir that was linked to 46 deaths in Panama, as well as to other deaths in Nigeria, India, South Africa, and Argentina. Those

cases were ominously reminiscent of a similar contamination 1996 that was associated with the deaths of 85 children in Haiti. In both cases, the sources of the substitution were reported to be Chinese drug manufacturers, as was the diethylene glycol contamination of toothpaste that was found recently in many countries, including the United States.[1]

- About 20% of drugs in the European Union are now purchased through their system of "parallel trade," meaning they can come from virtually anywhere; and in just the past 2 years, seizures alone of fake drugs in the EU went from 500,000 tablets to almost 3 million.
- A recent "sting" operation by the The Sunday Times of London set up a phony drug wholesaler, who was able to buy large quantities of counterfeit drugs from a Chinese manufacturer, who was reported to make pharmaceutical ingredients for legal sale by day and fake drugs for illicit sale by night. The Times reported that counterfeiters are increasingly turning from fake handbags and currency to drugs, because the drugs are so easy to make and sell on world markets.
- The World Health Organization has reported that in some areas of the world, particularly parts of Africa and Asia, more than one-half of the pharmaceutical supply is counterfeit. Indeed, drug counterfeiting is considered to be endemic around the world, with the United States thus far one of the few exceptions. China is alleged to be a principle world supplier of such products.

[1] Ironically, and sadly, it was diethylene glycol substitution for glycerin in an elixir that killed over 100 Americans in 1937 and led Congress to enact the Food, Drug and Cosmetic Act, and thus create the drug safety system that the United States relies upon today..

- Within China itself, the annual number of deaths from counterfeit and substandard drugs is reported to be between 200,000 and 300,000.

I could go on with numerous other examples, many of which would include a frequent reference to China. But I do not intend to suggest that "Made in China" should become a synonym for danger. That country's enormous economic development in recent years has made it the source around the world of increasing percentages of many nation's consumer goods. Here in the United States, it is estimated that 40% of all consumer products we purchase originate in China. Most are assuredly safe and an attractive bargain for Americans seeking to stretch their income as far as possible.

But drugs are not socks or running shoes. They are special, and Congress recognized their unique importance to health—and their potential risk—when it gave FDA the authority so many years ago to create a comprehensive regulatory system over pharmaceuticals. I believe FDA did its part, and did it well—by bringing to bear the best scientific knowledge of drug development and production to create rules and procedures for assuring that our drugs are safely manufactured. However, I believe that we may now be at a turning point at which our future actions will determine whether we will go the way of other countries or stay on the path that has served us so well.

IN WHAT DIRECTION ARE WE HEADED?

As the Committee has documented in hearings this year with respect to imports regulated by FDA, the United States has seen a massive change in sourcing of many foods and drugs in recent years. Today, perhaps two-thirds of our pharmaceuticals have foreign components, either as so-called "finished dosage form" -- the pill we get from the pharmacy; or Active Pharmaceutical Ingredient -- the active ingredient that is shipped to the United States for production of the final pill form. And that ratio is predicted to climb to 80% or more by the end of this decade. Yet in the face of this flood of drugs and drug ingredients from overseas, what are we doing to assure that they are as safe as drugs produced in this country? The facts are fairly dismal:

- FDA's inspection rate for imported drugs (and drugs ingredients) when they arrive at a U.S. port is around 1%, which means that the vast majority of imported drugs do not receive an FDA inspection upon entry into this country.
- The chances of an imported drug being sampled and tested at entry to this country is even lower; in fact, of the millions of drug shipments arriving from foreign countries last year, only 340 samples were taken for laboratory testing.
- Although there are approximately 3000 foreign drug manufacturers registered with the FDA, only 341 were inspected last year. And even that number is misleading, as most of those inspections were so-called "preapproval inspections" for drugs about to be approved by FDA for

marketing. The number of good manufacturing compliance inspections was perhaps two dozen or so.

- The Food, Drug and Cosmetic Act dictates that each drug manufacturer be inspected at least every two years, but the current rate of foreign inspections is infrequent at best. Please stop and think about that – we are buying ever larger percentages of our drug ingredients from producers in developing countries who receive virtually no FDA inspection, despite a statutory requirement that they be inspected regularly.
- The two biggest foreign suppliers of drug ingredients are China and India, both developing countries with weak regulatory systems over drug manufacturers; that have a track record of being the source for dangerous and substandard drugs; and in whose facilities FDA inspectors have at times found horrendous conditions.
- The information technology systems used by FDA to track registrations of foreign drug manufacturers and actual imports from those manufacturers are not linked and are so poorly coordinated that FDA inspectors often cannot tell if a firm actually importing a drug is even registered at all.

So, then, the question we must ask is where will we go as a nation, with respect to the safety of our pharmaceuticals. Will we accept the fact that drugs produced in many different countries, often in developing nations without a tradition of high standards, will be the main source for our health care and merely hope for the best? Or will we take the steps necessary to assure that these products are as safe as our scientists can make them?

THE GOOD NEWS

Unlike the circumstances with imported foods, for which the regulatory paradigm is clearly antiquated and dysfunctional, our drug regulatory system is not crying out for overhaul, for the following reasons:

1) Congress has provided FDA with a strong statutory construct for regulating the manufacturing of pharmaceuticals;

2) FDA has implemented that statute with effective, science-based regulations governing drug production;

3) Scientists within the Federal government, the pharmaceutical industry and academe have worked closely over the years to develop techniques for drug manufacturing and testing that have passed the test of time—that is, as a nation we are good at this and the rest of the world looks to us for leadership.

4) U.S. drug manufacturers accept the need for high standards in drug development and manufacturing and generally adopt those standards faithfully, including taking care to secure their chain of supply of drug ingredients.

5) Drugs made in the United States under FDA's rigorous quality control standards have an extraordinarily good safety record, as measured by the paucity of manufacturing defects and deaths and illnesses related to manufacturing deficiencies.

WHAT MUST BE FIXED

But there is one critical piece of the drug regulatory system that is broken, and must be corrected if we are to maintain our good safety record in drug production. That is the enforcement of the rules that govern drug production. It does no good to have rules if they are not obeyed, no good to set high standards if they are not used, and no good to develop advanced scientific skills if they are not employed. That countries such as China have a record of serious problems in drug manufacturing is indisputable. And the disparity in drug inspections – in which FDA inspects U.S. facilities regularly and those in China and India almost never -- is indefensible.

Some would say that we should not be buying products such as drugs from developing nations, but that flies in the face of the reality of global free trade. Others would rely upon agreements negotiated with foreign countries, under which those nations would assure the safety of drugs exported to the United States. I believe that a developing country is incapable of effectively implementing such an agreement, and that such a course of action is a prescription for frustration. In the end, I believe we must rely upon what we know has worked in the past to protect our drug supply – the FDA.

I believe FDA's scientists and regulatory officials are nothing short of terrific. They are well trained, intensely dedicated to the public health, and a true bargain for the American taxpayer. But they have been handed a task -- an expectation -- that they realistically cannot fulfill with their current resources. Simply put, they must be given two crucial things:

- Sufficient staff to do the work. FDA must have the people to examine and sample more imported drugs at the border, to dispatch inspectors to the facilities in other countries making these drugs, and to develop modern risk assessment techniques for gauging where and when to look for drug safety problems; and

- Funds for information technology. The agency's IT systems are woefully outdated, yet could make the oversight of imported drugs far more effective with a relatively small investment in funding. The IT systems should be configured in a way that allows the agency to use a myriad of risk factors, including potential impact on the public health, to direct its inspectional and import efforts. The import data system, for example, is so old and communicates so poorly with other FDA information systems that it is difficult for FDA officials to use risk as a predominant driver of their compliance efforts. Many of the data needs are obvious – such as what drugs are coming into the country from what manufacturers destined for what U.S. locations -- but the agency has been so starved for IT resources that it cannot do even some simple things with its current systems.

OTHER PRODUCTS

While I recognize that your focus for today's hearing is on prescription drugs, I would like to also briefly note that products other than foods and drugs are at risk from FDA's inability to adequately oversee imports. An ever increasing percentage of our over-the-counter drugs are being imported, often in final form without additional manufacturing in the United States. About two-thirds of our animal drugs are being made in China and

other developing countries, and FDA was able to conduct only 14 inspections of foreign animal drug facilities last year. And many Americans would likely be surprised to hear that a very large percentage – perhaps most – dietary supplements are produced in China as well (and a grand total of two of the foreign manufacturers of supplements received an FDA inspection last year).

I thank the Committee for holding this hearing today. Unfortunately, I was present for a similar hearing in this very room in 1986, and another in 2000. The concerns haven't changed all that much; but they're certainly more compelling than ever. I sincerely hope that this time your focus on this problem will result in some concrete action to help FDA protect our drug supply.

Thank you again for inviting me to give my views on this subject.